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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040319

Application Number: 09/783,320
Filing Date: February 15, 2001
Appellant(s): WALKE ET AL.

Lance K. Ishimoto
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10/20/2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

Appellant's brief includes a statement that there are no related appeals or interferences

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

Appellant's brief contains a statement indicating that there are no additional outstanding amendments.

(5) Summary of Invention

The summary of invention contained in the brief is substantially correct. However, it includes several statements in regard to the alleged uses of the present invention which are appropriately found in the argument's section of the Brief and will be addressed in the Response to Arguments section of this Answer.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The brief contains a statement indicating that claims in each of the issues shall stand or fall together as a group.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Bork, Genome Research, 10:398-400, 2000

Broun et al., Science 282:1315-1317, 1998

Letwin et al., EMBO J 11(10):3521-3531, 1992

Nagase et al., DNA Res. 8(4):179-187, 2001

Nagase et al., EMBL accession number Q96PY6, 2002

Seffernick et al. , J. Bacteriol. 183(8):2405-2410, 2001

Upadhya et al., Proc Natl Acad Sci 97(1):217-221, 2000

Van de Loo et al., Proc. Natl. Acad. Sci. 92:6743-6747, 1995

Witkowski et al., Biochemistry 38:11643-11650, 1999

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 4, 11 and 12 stand rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 4, 11 and 12 are directed to an isolated nucleic acid comprising a sequence which encodes the amino acid sequence of SEQ ID NO: 4, an expression vector and a host cell comprising said nucleic acid.

Appellants assert that the polypeptides encoded by the polynucleotides of the instant application share structural similarity to animal kinases (page 1, lines 33-35) and that these kinases include, but are not limited to, cell division control protein kinases, serine/threonine protein kinases, guanylate kinases (page 2, lines 1-5). Therefore, based on structural similarity, Appellants assert that the polynucleotides of

the instant application encode a novel kinase family of proteins having homologs and orthologs across a range of phyla and species.

While the specification does not state a specific biological function for the polypeptide of SEQ ID NO: 4 and the corresponding polynucleotide (SEQ ID NO: 3), it appears to assert that the polynucleotide of SEQ ID NO: 3 may encode a new human kinase. However, the claimed invention does not meet the utility requirements for the following reasons.

First, the specification provides no clue as to the type of kinase being encoded by the polynucleotide of the instant invention (SEQ ID NO: 3). Kinases belong to a large and diverse family with different specificities and substrates. As such, a statement indicating that the polypeptide of SEQ ID NO: 4 belongs to a novel kinase family is not sufficient for one of skill in the art to determine the actual function and consequently, the use of the protein (SEQ ID NO: 4) encoded by the polynucleotide (SEQ ID NO: 3) of the instant invention. In addition, neither Appellant's disclosure, nor the state of the art at the time the invention was made provides any guidance as to what the function of the polypeptide of SEQ ID NO: 4 is, its specificity, its substrate, or the biological processes associated with said polypeptide. No working examples have been provided either. There is no disclosure of critical structural elements in the polypeptide of SEQ ID NO: 4 which would allow one of skill in the art to identify the type of kinase the polypeptide of SEQ ID NO: 4 is, or its potential biological role. In addition, there is not even a disclosure of the protein kinase which shares the highest structural homology with the polypeptide of SEQ ID NO: 4, or the level of structural homology between such protein kinase the polypeptide of SEQ ID NO: 4, i.e. % sequence identity. In the absence of this information, it is unclear as to how one of skill in the art would determine (1) whether it is reasonable to conclude that the polypeptide of SEQ ID NO: 4 is a kinase based on the level of structural homology, and (2) the potential specific kinase activity associated with the polypeptide of SEQ ID NO: 4. Even if one assumes that the polypeptide of SEQ ID NO: 4 is a protein kinase based solely on structural homology, in view of the

complete lack of disclosure as to the type of kinase activity associated with the polypeptide of SEQ ID NO: 4, its specificity, its substrates, and the biological processes associated with said polypeptide, one cannot reasonably conclude that the specification discloses a specific utility associated with the alleged kinase of the instant invention.

The specification discloses that kinases are involved in a range of regulatory pathways and that given the physiological importance of kinases, they have been the subject of intense scrutiny and found to be drug targets (page 1, lines 25-28). The specification also asserts that the polynucleotides of the instant invention can be used to identify mutations associated with a particular disease (page 7, lines 35-37). Other asserted uses for the polypeptide of SEQ ID NO: 4 or the corresponding polynucleotide include identification of related cellular gene products, and screening for pharmaceutical reagents useful in the treatment of mental, biological or medical disorders/diseases (page 16, lines 10-15). In addition, the specification asserts that the polynucleotides of the instant application can be used as hybridization probes or in gene chips (page 5, line 30-page 7, line 34)

While the specification asserts several uses for the claimed polynucleotides, these utilities are not considered substantial and specific for the following reasons. The specification fails to disclose sufficient information in regard to the biological significance and further characterization of the claimed polynucleotides and the protein encoded thereby, such as (1) the targets (i.e. interacting proteins) of the alleged kinase, (2) the biological processes or pathways in which the targets or the polypeptide of SEQ ID NO: 4 are involved, (3) specific conditions/diseases associated with the expression, or lack thereof, of the polynucleotide of SEQ ID NO: 3, such that a specific use for the claimed polynucleotides would be apparent. If information in regard to the biological role of the claimed invention were to be presented, several utilities could be apparent for the claimed polynucleotides and the corresponding polypeptide, such as detection of the targets in samples, or isolation of modulators which can be used to regulate the processes in which the alleged protein kinase is involved. However, these utilities require additional

information which is not presented by the specification. As known in the art and admitted by Appellants in the specification, kinases are associated with many different biological processes. Furthermore, kinases belong to a large and diverse family of proteins with diverse roles in many physiological and pathological processes, therefore one would expect a protein kinase to be rather specific in regard to its targets. Since, the substrates, the cellular function of the kinase and its targets, and the biological processes associated with the targets/ kinase are all unknown, the utilities recited in the specification are not substantial since they will require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See e.g., *Brenner v. Manson,* 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The instant situation is analogous to the lack of substantial utility examples provided by MPEP § 2107.01 in that basic research is required to study the properties of the claimed polynucleotides and the corresponding polypeptide as well as the mechanisms in which the claimed polynucleotides are involved. In addition, while one could argue that some of the recited uses are specific, such as being a probe to be used in microarrays, it is noted that these uses are not specific due to the fact that all other human polynucleotides can be used as probes in microarrays. Since the instant specification does not disclose an specific and substantial "real world" use for the polynucleotide of SEQ ID NO: 3 or a polynucleotide encoding the polypeptide of SEQ ID NO: 4, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

Claims Rejections – 35 USC §112, first paragraph – Enablement

Claims 4, 11 and 12 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

A. Do Claims 2-3 and 6-7 lack patentable utility?

On page 4 of the Brief and continuing on page 5, Appellants state that the sequences of the present invention encode a human kinase protein and that this is apparent throughout the specification. Appellants assert that the sequences of the present invention encode a human variant of NEK-1. Appellants direct the Board's attention to Exhibit A, which discloses a sequence alignment between SEQ ID NO: 4 and the sequence disclosed by Nagase et al. (GenBank/EMBL accession number Q96PY6, 2002). Appellants submit that the polypeptide of Nagase et al. is 96.343% sequence identical to the sequence set forth in SEQ ID NO: 4 and has been annotated by third party scientists whole unaffiliated with Appellants as a human serine/threonine kinase NEK-1. Appellants also refer to the teachings of Letwin et al. (EMBO J 11(10):3521-3531, 1992; Exhibit B) and Upadhya et al. (Proc Natl Acad Sci 97(1):217-221, 2000; Exhibit C) in support of the argument that NEK-1 is known in the art, has utility, and a disease association. Appellants refer to studies in homozygous NEK-1 mutant animals which indicate that NEK-1 participates in signaling pathways to regulate cellular processes and the association between mutations in NEK-1 and kidney disease in mice. Therefore, according to Appellants, there can be no question that Appellant's asserted utility is credible.

First, it is noted that nowhere in the specification, there is an assertion that the polypeptide of SEQ ID NO: 4 encodes a human NEK-1 protein. As indicated above, all that is taught by the specification regarding a biological activity is that the polynucleotides of the instant application encode a novel kinase family of proteins having homologs and orthologs across a range of phyla and species. In addition, it is reiterated herein that nowhere in the specification, there is a disclosure of the polypeptide of Nagase et al. as a structural/functional homolog of the polypeptide of SEQ ID NO: 4, or its putative biological function. As it can be seen from the record, the polypeptide of Nagase et al. was first brought

to the Examiner's attention in the response filed 9/30/2002 to the Non Final Action mailed on 5/22/2002. Furthermore, nowhere in the specification, is there a teaching or suggestion regarding a correlation between the function of the mouse protein of Letwin et al., which is the only experimentally characterized NEK-1 protein known, and the polypeptide of SEQ ID NO: 4, or how the protein of Letwin et al. is structurally related to the polypeptide of SEQ ID NO: 4, e.g.. % sequence homology.

The Examiner acknowledges the teachings of Nagase et al., Letwin et al. and Upadhya et al. regarding (1) the high structural similarity between the polypeptide of SEQ ID NO: 4 (1214 amino acids long) and the polypeptide of Nagase, (2) the characterization of a mouse kinase labeled NEK-1 as a dual specificity kinase which is related to a kinase associated with cell cycle regulation, as taught by Letwin et al., and (3) the association between mutations in the NEK-1 gene and polycystic kidney disease in mice, as taught by Upadhya et al. However, the Examiner disagrees that these references support Appellant's contention that the claimed invention has utility or that the specification has described the claimed invention to the extent that one of skill in the art would know how to use the claimed invention. In regard to the teachings of Nagase et al., it is reiterated herein that Nagase et al. does not provide any experimental corroboration that the polypeptide is indeed a human NEK-1 protein kinase. Nagase et al., like Appellants, assigned a putative function to the polypeptide disclosed based solely on structural homology. This is evidenced by the teachings of Nagase et al. (DNA Res. 8(4):179-187, 2001), which is cited in GenBank's entry Q96PY6 under Reference 1. Nagase et al. (DNA Res. 8(4):179-187, 2001) teaches the prediction of 60 cDNA clones from brain which code for large proteins, including GenBank's entry Q96PY6.

As such, the annotations of Nagase et al. are based on virtually the same information as are the assertions made by Appellants in the Brief and add nothing to the record in support for Appellant's position. It is also noted that the only experimentally determined NEK-1 protein, i.e. the mouse NEK-1 protein of Letwin et al. (774 amino acids long), is at best 54% sequence identical to the polypeptide of

SEQ ID NO: 4 (665 matches; 54%=665x100/1214). See alignment. The skilled artisan would find this level of homology sufficient to support an assertion that the protein of SEQ ID NO: 4 is a kinase but would not find it sufficient to support an assertion that the protein of SEQ ID NO: 4 shares the same substrates and biological functions as the protein of Letwin et al. Furthermore, as previously noted, the specification does not make the specific assertion that the polypeptide of SEQ ID NO: 4 is a NEK-1 kinase. Thus, at best a skilled artisan would believe that the polypeptide encoded by the claimed polynucleotides could be placed in the broad general class of kinases but no specific function beyond that can be presumed absent a disclosure of the critical structural elements which are characteristic of NEK-1 proteins present in the polypeptide of SEQ ID NO: 4. Therefore, while one could reasonably conclude that a human NEK-1 protein may have a similar biological role to that characterized by Letwin et al. and Upadhya et al. in mice, in view of the uncertainty in regard to the real function of the polypeptide of SEQ ID NO: 4 and the polypeptide of Nagase et al., and the unpredictability of the art in regard to assigning function based solely on structural homology, it is not reasonable for one of skill in the art to conclude that Appellant's polynucleotides have a specific and substantial or well-established utility.

On page 5 of the Brief and continuing on page 6, line 16, Appellants refer to the teachings of Bork (Genome Research, 10:398-400, 2000), Broun et al. (Science 282:1315-1317, 1998), Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995), Witkowski et al. (Biochemistry 38:11643-11650, 1999), Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001), presented by the Examiner in the Final Action mailed on 12/17/2002 and the Advisory Action mailed on 5/20/2003, which were introduced by the Examiner in support of the argument that structural homology is not sufficient to assign function. Appellants indicate that Bork's citation of his previous work and not the work of others should cast doubt on the broad applicability of Bork's position. Appellants refer to Table 1 on page 399 of Bork (Genome Research, 10:398-400, 2000) to indicate that the accuracy of the methods used by Appellants are high. Appellants also submit that Bork (Genome Research, 10:398-400, 2000) does not teach a comparison of

the prediction accuracy based on the % homology between two proteins or two classes of proteins. Appellants refer to the 98% accuracy for "Homology" and 90% accuracy for "Functional features by homology" shown in Table 1 as high numbers which should support Appellant's assertion. Appellants argue that the teachings of Bork (Genome Research, 10:398-400, 2000) clearly indicate that there is value in sequence analysis and that there is room for improvement.

As indicated in the Final Rejection mailed on 12/17/2002, Bork (Genome Research, 10:398-400, 2000) teaches that protein function is context dependent, and both molecular and cellular aspects should be considered (page 398). The Examiner acknowledges Table 1, the use of previous references by Bork in the instant reference, and Bork's statement regarding the power of sequence analysis and the need for improvement. However, the Examiner disagrees with Appellant's contention that the teachings of Bork do not support the notion that accurate protein function assignment based solely on structural homology is unpredictable. First, it is unclear as to how the use of other references by the same author in support of the teachings disclosed in the instant reference should cast doubt on the teachings of Bork (Genome Research, 10:398-400, 2000), particularly in view of the references presented by the Examiner (Broun et al., Van de Loo et al., Seffernick et al. and Witkowski et al.), which are examples of how protein function prediction based on structural homology was proven inaccurate. These references further support Bork's position regarding the unpredictability of assigning function based on structural homology. In regard to the teachings of Table 1, it is noted that such Table discloses selected examples of prediction accuracy in different areas of sequence analysis. The percent accuracy disclosed is in reference to a specific data set (i.e. reference set; column 4). In the case of "Homology (several methods)", the 98% accuracy value disclosed is in reference to a specific reference data set, which is one disclosed by Muller et al. as stated in column 5 of Table 1. In regard to "Functional features by homology", it is noted that the 90% accuracy value is in reference to a reference set containing unicellular genomes, which is disclosed by Bork and Koonin, as stated in column 5 of Table 1. Therefore, Bork does not teach that prediction of homology or

functional features by homology is 98% or 90% accurate for all proteins known. Instead, these values are specific to the reference data set shown in column 4 of Table 1. Also, it is important to note Bork 's statement indicating that the numbers in Table 1 are often overestimates because the test sets used are usually not representative of all sequences (page 400, left column, last paragraph; Taking the 70% hurdle). As such, the teachings of Bork (Genome Research, 10:398-400, 2000) in no way support Appellant's assertions as claimed above. In regard to the teachings of Bork (Genome Research, 10:398-400, 2000) indicating the power of sequence analysis, it is not the Examiner's contention that one of skill in the art would not recognize the usefulness of bioinformatic predictions. However, as indicated by Bork throughout the article, there are limitations in the use of computational prediction of function, particularly in view of the fact that the analysis methods used in such predictions are knowledge-based and the quality of data in public sequence databases is still insufficient (page 398, middle column, first paragraph).

On page 6 of the Brief, line 16, and continuing on page 7, Appellants refer to the teachings of Broun et al., Van de Loo et al., Seffernick et al. and Witkowski et al. as additional single rare examples of non-kinases where function assignment were proven to be incorrect. According to Appellants, these examples are hardly indicative of a high level of uncertainty and do not support the alleged lack of utility. Appellants agree that there is no 100% consensus within the scientific community as to the accurate prediction of function from homology information and further agree that protein function prediction is not 100% accurate. However, Appellants indicate that 100% accuracy in protein function prediction is irrelevant to the question of whether the claimed invention has utility and submit that this is not the standard for patentability under 35 USC 101. It is Appellant's contention that all that is required is an assessment of whether one of skill in the art would find any of the utilities described to be believable, and that an overwhelming majority of those skilled in the art would believe prediction of protein function from homology information and the usefulness of bioinformatic information. As such, Appellants submit that an overwhelming majority of those skilled in the art would believe that Appellant's protein is a

kinase protein NEK-1, whose function has been described. Since the standard for meeting the utility requirement is "believability" and not "100% consensus or 100% accuracy", Appellants submit that the claims meet the requirements under 35 USC 101.

While the Examiner acknowledges that the teachings of Broun et al., Van de Loo et al., Seffernick et al. and Witkowski et al. do not involve a kinase, it is noted that these references were introduced by the Examiner as individual examples which support Bork's teachings regarding the unpredictability of annotating function based solely on structural homology. As indicated in previous Office Actions, Witkowski et al. teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Van de Loo et al. teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* were found to be hydroxylases once tested for activity. Seffernick et al. teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. The references by Broun et al., Van de Loo et al., Seffernick et al. and Witkowski et al. teach specific examples of enzymatic activity which was mistakenly predicted by structural homology, and are evidence of the general state of the art in regard to function annotation based on structural homology (i.e. sequence homology), as disclosed by Bork. As such, contrary to Appellant's assertion, these examples are highly indicative of the high level of uncertainty in the art regarding the accurate prediction of protein function based on structural homology alone.

The Examiner is not contending that (1) the standard for patentability under 35 USC 101 is 100% accuracy or 100% consensus, (2) one of skill in the art would not recognize the usefulness of bioinformatic predictions, (3) there are not instances where function has been accurately predicted based

on structural homology, or (4) structural homology is never sufficient for one of skill in the art to believe an assertion of function based thereon. However, as taught by the art presented by the Examiner, at the present time, with the tools currently available, there is no general consensus as to which genes are going to be easier to annotate using structural homology or which are the conditions required for functional annotation using structural homology to be highly predictable for any gene, except for the level of structural homology. As shown by the examples provided by the Examiner, even structural homologies ranging from about 60% to 98% have been found to be not sufficient to accurately predict function in all instances. While the Examiner has presented examples where even 1 amino acid substitution can result in a different function, one of skill in the art is more likely to conclude that a particular polynucleotide encodes a protein of a certain function if the functional homologs have a high degree of structural (i.e. sequence) similarity or if certain motifs specific to that function are present. In the instant case, however, the polypeptide of Letwin et al., which is the closest experimentally determined functional homolog of the polypeptide of SEQ ID NO: 4, is at best 54% sequence identical and the specification is silent in regard to which are the structural elements (i.e. motifs) in the polypeptide of SEQ ID NO: 4 that are associated to NEK-1 activity. As such, at best, one of skill in the art can agree that the claimed polynucleotides encode a kinase, but no specific functional characterization of this kinase can be made in the absence of any disclosure as to those motifs in the polypeptide of SEQ ID NO: 4 which are characteristic of NEK-1 proteins. As kinases are such a broad class of proteins with such a wide variety of distinct utilities, disclosure of a specific functional characterization is necessary for disclosure of a specific utility. Without any knowledge as to the type of kinase, a skilled artisan would not know how to use a new kinase as the artisan would not know what compound could be phosphorylated or what diseases or cellular processes are likely to be regulated. While kinases have been associated with many cellular processes, not all members of the kinase family are associated with the same diseases/cell processes. The specification fails to provided this necessary specificity.

On page 7 of the Brief, and continuing on pages 8-9, Appellants argue that not even the PTO requires 100% identity between proteins to establish functional homology and that the Examiner's position is contrary to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials in view of the 95% similarity score to a protein of known function. According to Appellants, the instant situation is identical to the case presented in Example 10. Appellants submit that it is clear that the sequences of the present invention encode a novel human kinase, specifically NEK-1, for which there is a well established utility recognized by those of skill in the art. Appellants indicate that protein kinases have a well-established use in the molecular biology art based on their ability to phosphorylate proteins at serine and threonine residues. Therefore, in view of their well-established utility, the claimed invention also meets the utility requirement. According to Appellants, one of skill in the art would appreciate the utilities asserted by Appellants regarding the role of the proteins encoded by the polynucleotides of the instant inventions, including those associated with diseases that have been linked to the novel human kinase proteins.

The Examiner acknowledges (1) Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials, and (2) that serine/threonine protein kinases phosphorylate serine/threonine residues, but disagrees with Appellant's contention that the present case is identical to Example 10 or that there is a well-established utility for the polypeptide of SEQ ID NO: 4. In regard to Example 10, it is noted that the conclusion reached as to the utility of the claimed polynucleotide is based on the fact that the specification teaches which are the structural elements in the polypeptide encoded by the claimed polynucleotides which are also present in other known DNA ligases, i.e. consensus sequence disclosed, and the fact that such polypeptide contained a large number of such structural elements which are found in DNA ligases as evidenced by the high degree of structural similarity between the consensus disclosed and the structure of the polypeptide of Example 10, i.e. 95% similarity score. In the instant case, the specification provides no clue as to which are the structural elements which are present in other known

NEK-1 proteins which are also present in the polypeptide of SEQ ID NO: 4 (i.e. no consensus sequence or motifs disclosed), and the closest experimentally determined NEK-1 protein of Letwin et al. is only 54% sequence identical to the polypeptide of SEQ ID NO: 4. It is reiterated herein that while it is agreed that the polypeptide of Nagase et al. is highly homologous to the polypeptide of SEQ ID NO: 4, there is no experimental evidence which demonstrate that the polypeptide of Nagase et al. is indeed a NEK-1 protein. Since Nagase et al. uses structural homology to annotate function of the protein, one cannot reasonably conclude that such protein is a NEK-1 protein in view of the unpredictability of the art regarding accurate annotation of function based solely on sequence homology, as already discussed above. Also, as indicated above, based on the teachings of Letwin et al., at best, one of skill in the art can only conclude that the claimed polynucleotides encode a kinase but any determination as to whether the polypeptide is a NEK-1 protein cannot be made in the absence of any additional information as to those structural elements which are characteristic of NEK-1 proteins or experimental evidence demonstrating such activity. Thus, contrary to Appellant's assertion, the instant case is not identical to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials. Furthermore, it should be noted that the assertion of utility in Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials is specific, i.e. the assertion is of a DNA ligase (not just a ligase), such that one would know how to use the protein from the assertion. In the instant case, the specification merely asserts kinase activity. This assertion is not specific enough for one of skill in the art to know how to use it. Even assuming that the specification asserts serine/threonine protein kinase activity, this is still not specific as one would still not know what protein is being phosphorylated.

In regard to the well-established utility of protein kinases, while it is agreed that the basic molecular function of a kinase is to phophorylate a substrate, as known in the art, the identity of the target substrate and where the target substrate is phosphorylated is of biological importance. In the case of proteins, different proteins phosphorylated by a kinase, or proteins phosphorylated at different residues,

may participate in different signaling pathways and regulate different cellular processes. Since in the instant case, the specification is completely silent in regard to the identity of target substrates, specific residues being phosphorylated by the alleged kinase, or biological processes associated with the alleged kinase, one cannot reasonably conclude that there is a well-established utility for the polypeptide of SEQ ID NO: 4. Moreover, it is reiterated herein that characterization of the polypeptide of SEQ ID NO: 4 as a human NEK-1 is nowhere to be found in the specification. Appellant's arguments in regard to the utilities disclosed which are associated with diseases linked to the novel human kinase proteins, it is noted that the specification provides no clue as to a specific disease associated with the polypeptide of SEQ ID NO: 4, whether excess or limited amounts of this polypeptide are responsible for a disease, or whether a mutation in the polynucleotide of SEQ ID NO: 3 is responsible for a specific disease. It is worth noting that while Appellants refer to the teachings of Upadhya et al. regarding an association between a mutation in the mouse NEK-1 protein and polycystic kidney disease, nowhere in the specification there is disclosure of an association between polycystic kidney disease and the polypeptide of SEQ ID NO: 4.

On page 9 of the Brief and continuing on page 10, Appellants point out that the knowledge of the exact function or role of the claimed polynucleotides is not required to track expression patterns in a DNA chip. According to Appellants, given the widespread utility of gene chips which use public domain gene sequence information, there can be little doubt that the use of the claimed invention would have great utility in such DNA chip applications. Appellants submit that the claimed invention provide a specific marker of the gene encoding the human kinase NEK-1 and provide a unique identifier. Appellants assert that the claimed polynucleotides are ideal candidates for assessing gene expression in DNA chips. Appellants submit Exhibits D-I which disclose US patents related to DNA chip technology in support of the argument that DNA chips have utility. Appellants argue that even negative information has great "real world" practical utility in that knowing which genes are not expressed in medically relevant tissue allows for the more efficient deployment of expensive drug discovery resources. Appellants indicate that

the utility of DNA chips is enhanced by addition of the claimed polynucleotides and that the claimed polynucleotides provide a specific tool for identifying and quantifying full length transcripts. According to Appellants, additional disclosure of the tissues which express the claimed polynucleotides along with evidence that the present polynucleotides encode a kinase protein demonstrate the outstanding utility of the claimed polynucleotides in DNA chip expression analysis.

While it is agreed that (1) public domain gene sequence information is used in gene chip applications, (2) knowing that a given gene is not expressed in certain tissues provides useful information, (3) tracking gene expression does not require knowing its biological function, and (4) many patents related to gene chip technology, such as those in Exhibits D-I have been issued, the Examiner disagrees with Appellant's contention that the claimed polynucleotides have patentable utility in gene chip applications since they are specific markers which can be used to assess gene expression or to identify/quantify full length transcripts from the corresponding genomic locus. The Examiner is not disputing the patentable utility of DNA chips as a collection of polynucleotides linked to a solid support but rather the patentable utility of specific polynucleotides encoding an alleged kinase protein. The Examiner acknowledges the hundreds of issued patents in regard to DNA chips however it is noted that the instant claims are not drawn to methods of use of DNA chips or to DNA chips (microarrays) but rather to specific polynucleotides. Furthermore, the asserted use of the claimed polynucleotides in DNA chips is not specific since as Appellants have stated, many other polynucleotides including those in the public domain can and are used in DNA chips. As indicated by the Examiner in previous Office Actions, for the claimed polynucleotides to be specifically useful in DNA chip applications, one would require some knowledge or guidance as to the biological role of the polypeptide encoded by such polynucleotides to effectively use the information gathered in tracking the expression patterns of such polynucleotides. The reduction or increase in expression of a polynucleotide, or the identification/quantification of full length transcripts from the corresponding genomic locus, are meaningless unless one can link changes in

expression, or the detection of transcripts, with some biological function. For example, if one were to use the claimed polynucleotides in assays which would lead to the discovery of drugs for a specific condition, such as an assay which uses a DNA chip to evaluate expression patterns upon exposure to a test compound, one needs to know which diseases and/or biological functions are associated with the expression of such polynucleotides. Otherwise, one of skill in the art would have to carry out further experimentation to determine which are the conditions (i.e. diseases) and/or biological functions associated with the claimed polynucleotides. Appellant's contention that the claimed polynucleotides have patentable utility in gene chip applications since they are specific markers which can be used to assess gene expression or to identify/quantify full length transcripts from the corresponding genomic locus is not persuasive since the specification is completely silent as to how one of skill in the art can use the information gathered by assessing gene expression or identifying/quantifying full length transcripts in some meaningful way, such as diseases associated with the expression, or lack thereof, of the claimed polynucleotide, and/or levels of expression which are indicative of disease. This is analogous to the examples provided by MPEP § 2107.01 in regard to what constitutes carrying out further research to identify or reasonably confirm a "real world" context of use since basic research is required to determine the properties or the mechanisms in which the claimed product is involved. Therefore, it is unclear how one of skill in the art can reasonably conclude that the asserted use of the claimed polynucleotides in DNA chips is a specific and substantial utility.

On page 10 of the Brief, first paragraph, Appellants submit that only a small percentage of the genome encodes exons. Thus, according to Appellants, not all human genomic DNAs are useful in gene chip applications. Therefore, it is Appellant's opinion that this is evidence which shows that such uses are not generic, as asserted by the Examiner. Appellants further cite *In re Langer* and *In re Marzocchi* to support the argument that a statement of utility in a specification must be accepted absent reasons why one of skill in the art would have reason to doubt truth of such statement.

While the Examiner agrees that only a small portion of the genome encodes proteins, as admitted by Appellants, other polynucleotides comprising exons can be used in gene chips. Furthermore, as known in the art, gene chips can comprise polynucleotides which do not comprise exons. As indicated above and reiterated herein, for the claimed polynucleotides to be specifically useful in DNA chip applications, one would require some knowledge or guidance as to the biological role of the polypeptide encoded by such polynucleotides to effectively use the information gathered in tracking expression patterns. In regard to the findings in *In re Lager* and *In re Marzocchi*, it is noted that credibility has not been assessed. The Examiner deemed the claimed invention as lacking utility in view of the fact that the claimed polynucleotides do not have a specific and substantial or well-established utility, for the reasons discussed above.

On page 10 of the Brief, last paragraph, Appellants argue that evidence of "real world" substantial utility is further provided by the fact that there is an entire industry based on the use of genes or fragments thereof in a gene chip. Appellants refer to many companies known to use gene chip technology and assert that in view of the fact that these companies are worth millions of dollars, there is a "real world" substantial industrial utility associated with such genes and fragments thereof. Appellants further indicate that persons of skill in the art as well as venture capitalists would readily recognize the utility of genomic data, especially human. Appellants refer to Exhibits J (Venter et al.) and K (Jasny et al.) in support of the argument that billions of dollars have been spent in the human genome project and that the results have been a stunning success since the utility of the genomic data has been widely recognized as a great gift to humanity. Appellants conclude that the usefulness of human genomic data such as what is disclosed by the specification is substantial, credible and well-established.

While the Examiner acknowledges that (1) there is an entire industry based on the use of gene chip technology, (2) many companies using this technology are worth millions of dollars, (3) one of skill in the art as well as venture capitalist and investors can recognize the utility of genomic data,(4) the

teachings of Venter et al. and Jasny et al, (5) billions of dollars have been spent in the generation of human genomic data, (6) the utility of human genomic data, Appellant's arguments have not been found persuasive for the following reasons. First, it is noted that commercial success is not one of the requirements for utility under 35 USC § 101. The Examiner is not disputing that one of skill in the art can see the potential usefulness of information coming out of the human genome project, however it is also known in the art that this information is valuable to the extent that it provides a starting point for scientists to further investigate the biological significance of the genetic information collected and possibly discover how to treat many conditions and diseases. In fact, while the potential usefulness of human genomic data was enormous, the lack of an immediate use for human genomic data was the primary reason why it was the federal government and not a private entity who first provided funding for the Human Genome Project. While it is agreed that the disclosure of an additional human polynucleotide provides more information in regard to the human genome, as indicated previously, in the absence of any additional information in regard to its biological function, the isolation of the human polynucleotides of the instant application is only useful as a starting point for researchers to further investigate its biological significance, therefore the utility of the instant polynucleotides, as clearly stated in MPEP § 2107.01 is not a "real world" substantial utility.

On page 11 of the Brief, first paragraph, and continuing on page 12, Appellants submit that given the physiological activity and importance of kinase proteins and NEK-1, one of skill in the art would recognize the importance of tracking expression of the genes encoding the described protein. According to Appellants, once the role of the sequence has been identified, nucleic acid sequences have the greatest specific utility and the level of gene expression is of greater significance. Appellants submit that the specific utility is distinct from the requirement for a unique utility. According to Appellants, the fact that other nucleic acids find utility in gene chip applications does not mean that Appellant's use of the claimed polynucleotides in gene chip applications is not a specific utility, and cite *Carl Zeiss Stiftung v. Renishaw*

PLC, 20 USPQ2d 1101 (Federal Circuit 1991) in support of their arguments. Appellants argue that the proper standard for utility under 35 USC § 101 is specific and not unique and that if every invention were required to have unique utility, the PTO would no longer be issuing patents on batteries, automobile tires, golf balls, golf club and treatments for a variety of human diseases because examples of each of these have already been described and patented. Furthermore, it is Appellant's opinion that if a composition needed to be unique to be patented, the entire class/subclass system would be an effort in futility.

While it is agreed that at least in mice, the NEK-1 protein appears to have an association with polycystic kidney disease, the Examiner disagrees with the notion that a similar function and disease association can be extrapolated to the polypeptide of SEQ ID NO: 4 in the absence of any experimental corroboration indicating whether the polypeptide of SEQ ID NO: 4 is a NEK-1 protein. If the polypeptide is indeed a human NEK-1 protein, it would not be unreasonable to suspect a similar disease association for the human NEK-1 protein, i.e. polycystic kidney disease and mutation of the NEK-1 protein. If it is demonstrated that the polypeptide of SEQ ID NO: 4 is a human NEK-1 protein and it is found that there is an association between polycystic kidney disease and a mutation in the polypeptide of SEQ ID NO: 4, Appellant's use of the claimed polynucleotides in gene chip applications would be a patentable utility since tracking gene expression or detecting transcripts could be correlated to a specific biological function and disease. However, in the instant case, there is no evidence presented in the specification which shows (1) the polypeptide of SEQ ID NO: 4 being a human NEK-1 protein, and (2) an association between the polypeptide of SEQ ID NO: 4 and polycystic kidney disease or any specific disease. Furthermore, it is noted that while the teachings of Upadhya et al. indicate a mutation in the gene of NEK-1 as the potential cause of progressive polycystic kidney disease in mice, Appellant's disclosure provide no clue as to which mutation in the polynucleotide of SEQ ID NO: 3 or in the gene encoding said polypeptide is associated with the disease in humans.

The Examiner acknowledges the findings in *Carl Zeiss Stiftung v. Renishaw* PLC and agrees that the legal standard under 35 USC § 101 is specific and not unique. The Examiner is not contending that the claimed polynucleotides lack utility because other polynucleotides have been used previously in gene chip applications but rather due to the fact that the use of the claimed polynucleotides in gene chip applications is neither specific nor substantial. The specification provides no information or guidance as to the specific biological function and/or disease associated with changes in expression patterns or the detection/identification of transcripts. The asserted utility in gene chip applications is not a substantial utility in view of the fact that additional research is needed to identify which biological function and/or diseases correlate with the expression, or lack thereof, of the claimed polynucleotides.

On page 12 of the Brief, and continuing on page 13, Appellants argue that while only one utility is needed to meet the requirements of 35 USC § 101, the claimed polynucleotides have specific utility in determining the genomic structure of the corresponding human chromosome and for mapping the protein encoding regions. Appellants submit that the claimed polynucleotides provide exquisite specificity not shared by virtually any other nucleic acid. Appellants state that early gene mapping techniques do not provide sufficient resolution to detect specific genes involved in disease and that a significant benefit is afforded by the claimed polynucleotides as markers of a specific locus of the human genome.

The Examiner acknowledges that (1) earlier mapping techniques may not provide high resolution, and (2) the claimed polynucleotides can be used to detect a human chromosome and a particular locus within that human chromosome. However, the Examiner disagrees with Appellant's contention that the claimed polynucleotides have utility for the following reasons. First, the specification is completely silent as to which human chromosome contains the claimed polynucleotide. Even if the human chromosome which contains the polynucleotide of SEQ ID NO: 3 is known, while the polynucleotide of SEQ ID NO:3 can be used as a marker to detect the corresponding human chromosome since such chromosome contains the locus of the gene encoding the polypeptide of SEQ ID NO:4 (encoded by the polynucleotide of SEQ

ID NO:3), that chromosome also contains other genes. As such, any polynucleotide which is complementary to any of those genes can be used as a marker of such chromosome. Similarly, any of those genes contained in that chromosome can be used for gene mapping and would also have the ability to localize a particular region of such chromosome. Therefore, unless there is some information as to the biological role and/or the conditions/disorders associated with that particular locus in that human chromosome, or some information is provided in regard to how the claimed polynucleotides are specific markers of the human genome, the asserted uses of the claimed polynucleotides cannot be considered specific and substantial.

On page 13 of the Brief, first paragraph and continuing on page 14, Appellants indicate that only a minor percentage of the genome actually encodes exons. As such, the claimed polynucleotides provide biologically validated empirical data that specifically defines that portion of the corresponding locus that actually contains an exon. Appellants also submit that the claimed polynucleotides define how the exons are spliced together to produce an active transcript. Therefore, according to Appellants, the claimed polynucleotides have practical scientific value in regard to the significance of expressed sequence information for structural analysis, as evidenced by Venter et al. Appellants further submit Exhibit L which shows an alignment of the polynucleotide of SEQ ID NO: 3 and human genomic DNA encoding the polypeptide of SEQ ID NO: 4 in support of the argument that the claimed polynucleotides have specific utility in localizing the specific region of the human chromosome and the identification of functionally active intron/exon splice junctions. Appellants submit that the polypeptide of SEQ ID NO: 4 is encoded by 31 exons along a region of human chromosome 4, and that this result has been corroborated by a party unaffiliated with Appellants (Nagase et al.). Appellants argue that those of skill in the art would recognize that when a polynucleotide encoding a protein is mapped onto a genomic sequence, those areas where the sequence of that polynucleotide is non-contiguous indicate exon/intron boundaries. Thus, it is Appellant's conclusion that this provides empirical evidence supporting

Appellant's assertions regarding the utility of the claimed polynucleotides in identifying functionally active intron/exon splice junctions.

The Examiner acknowledges that (1) only a minor percentage of the genome actually encodes exons, and (2) information regarding expressed polynucleotides is of great importance in structural analysis of genomic data. However, it is noted that it is the patentable utility of specific polynucleotides encoding an alleged protein kinase and not the significance of additional information in regard to additional coding sequences which is being determined and discussed.

In regard to Exhibit L as evidence which shows that the claimed polynucleotides have a patentable use in detecting a specific region of the chromosome and intron/exon splice junctions, it is worth noting that the specification does not provide any information as to the actual genomic locus (i.e. chromosomal position of the gene) which corresponds to the claimed polynucleotides. Exhibit L is an alignment of the polynucleotide of SEQ ID NO:3 and fragments of chromosome 4 which were disclosed by different parties after the instant application was filed. While it is agreed that (1) the alignment of Exhibit L appears to indicate that chromosome 4 contains the polynucleotide of SEQ ID NO: 3 at position 4q32.3, (2) the claimed polynucleotides can be used to map the corresponding locus in a human chromosome, which in this case appears to be chromosome 4, and (3) one would not be able to map the region of such chromosome containing the claimed polynucleotides without knowing the sequence disclosed in the specification, the Examiner disagrees with Appellant's contention that (1) there is a specific and substantial utility for the claimed polynucleotides for mapping specific regions of the chromosome or identification of intron/exon splice regions, and (2) the teachings of Nagase et al. further support Appellant's position in regard to the polypeptide of SEQ ID NO: 4 being a human NEK-1 protein. Any human polynucleotide which encodes a protein can be used to detect the particular locus of the corresponding gene, therefore any human polynucleotide which encodes a protein can be used to detect exons, intron/exon junctions, as well as to determine the specific chromosome which contains that

locus. In addition, while one could argue that the claimed polynucleotides can be used as markers to isolate the particular chromosome which contains the locus of the gene encoding the polypeptide of SEQ ID NO: 4 (encoded by the polynucleotide of SEQ ID NO:3), since that chromosome will contain many other genes, any polynucleotide which is complementary to any of those other genes will also serve as a marker for that particular chromosome. Therefore, one cannot conclude that the asserted utilities are specific to the claimed polynucleotides. This situation is analogous to the examples provided in MPEP § 2107.01 in regard to what constitute a non-specific utility since, as stated MPEP § 2107.01 "a specific utility is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to a broad class of inventions". Therefore, unless there is some information as to the biological role and/or the conditions/disorders associated with that particular locus in chromosome 4 or specific intron/exon splice junctions, the asserted uses of the claimed polynucleotides cannot be considered specific. It is reiterated herein that the specification never disclosed the polypeptide of SEQ ID NO: 4 as a NEK-1 protein kinase and the teachings of Nagase et al. (published after filing of the instant application) do not provide any additional information to the record regarding the actual specific biological activity of the polypeptide of SEQ ID NO: 4 in view of the fact that Nagase's annotation of function is purely based on structural homology and neither the specification nor the art provide any additional corroboration of this prediction. In the absence of any additional information in regard to its biological function, the isolation of the human polynucleotides of the instant application is only useful as a starting point for further experimentation and research. As such, the asserted utilities for chromosomal/gene mapping and detection of intron/exon junctions cannot be considered specific and substantial utilities.

In regard to arguments that the disclosure of the claimed polynucleotides provide biologically validated empirical evidence supporting Appellant's assertion of utility, it is noted that the specification provides no information as to how the mRNA was obtained, whether these polynucleotides were

identified in a cDNA library from these cells or how this cDNA library was constructed. As known in the art, cDNA libraries can contain cDNAs which may not be representative of the actual transcript of a gene (i.e. mRNA) since the PCR primers used in the construction of such libraries may contain parts of an intron and many other artifactual constructs can be produced during amplification of a library. As such, the cDNAs produced, while containing exons, may not be representative of an actual transcript as they may also contain parts of an intron or present artifactual junctions which are not naturally produced, therefore resulting in a wrong transcript of a gene. In the absence of additional experimental evidence corroborating that the claimed polynucleotides are indeed actual transcripts of a gene, one cannot reasonably conclude that the claimed polynucleotides provide biologically validated data. However, even if it is assumed that the claimed polynucleotides are indeed the actual transcript of a gene, as indicated previously, in the absence of any additional information in regard to its biological function, the isolation of the human polynucleotides of the instant application is only useful as a starting point for researchers to further investigate its biological significance, therefore the utility of the instant polynucleotides, as clearly stated in MPEP § 2107.01 is not a "real world" substantial utility.

On page 14 of the Brief, last paragraph, and continuing on page 15, Appellants argue that the Federal Circuit in *Juicy Whip Inc. v. Orange Bang, Inc.* has stated that the threshold of utility is not high and that an invention is useful under section 101 if it is capable of providing some identifiable benefit. Appellants further cite *Brooktree Corp. v. Advanced Micro Devices, Inc.* to indicate that the Federal Circuit has stated that a claimed device must be totally incapable of achieving a useful result to lack utility under 35 USC § 101. Appellants cite *Cross v. Iizuka* in support of the argument that any utility for a claimed invention is sufficient to satisfy the requirements of 35 USC § 101 and indicate that the Federal Circuit has confirmed that anything under the sun made by man is patentable in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.*

The Examiner acknowledges the numerous cases cited by Appellants wherein issues in regard to 35 USC § 101 were examined. It is noted however that only *Cross v. Iizuka* is considered relevant to the instant discussion since the inventions in that case are chemical compounds. In *Juicy Whip Inc. v. Orange Bang, Inc.,* the issue of utility was discussed in regard to a juice dispenser, *in Brooktree Corp. v. Advanced Micro Devices, Inc.,* the issue of utility was discussed in regard to a digital to analog conversion circuitry, and in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.,* the issue of utility was discussed in regard to a business method.

In *Cross v Iizuka*, the issues which the Federal Circuit had to examined were whether the Board erred in finding that the utility disclosed in the Japanese priority application by Iizuka is sufficient to meet the practical utility requirement of 35 U.S.C. §101 and whether the Board erred in finding that the Japanese priority application contained sufficient disclosure to satisfy the enablement, i.e., how-to-use, requirement of 35 U.S.C. § 112. The PTO, the Board of Patent Appeals and Interferences and the Federal Circuit found that the claimed imidazole derivative compounds had practical *in vitro* utility since in addition to the disclosure of the structure of the claimed imidazole derivative compounds, there was experimental evidence of the strong inhibition of thromboxane synthetase by these imidazole derivatives in human and bovine microsomes. Thromboxane synthetase is an enzyme which leads to the formation of thromboxane A 2, which at the time the applications of Cross and Iizuka were filed, was postulated to be a causal factor in platelet aggregation, which in turn, is known to be associated with platelet thrombosis, pulmonary vasoconstriction or vasospasm, inflammation, hypertension, and collagen-induced thrombosis. In contrast, the instant application discloses the structure of the claimed polynucleotides and no biological characterization of the polypeptide encoded by the claimed polynucleotides other than to state that based on sequence homology it appears to be a novel protein kinase. For the reasons indicated above, even if one assumes that the polypeptide encoded by the claimed polynucleotides is a protein kinase, the specification fails to provide sufficient information for one of skill in the art to know

how to use the claimed invention. The specification is silent in regard to (1) the specificity of the alleged protein kinase, i.e. target, (2) the biological processes or pathways in which the alleged protein kinase, or its target, are involved, or (3) the disorders or conditions associated with the alleged protein kinase, or its target. Information in regard to biological function and/or condition/disorders associated with the alleged kinase is essential for the asserted utility in DNA chips or gene mapping to be specific and substantial for the reasons already discussed above. While one of skill in the art can reasonably conclude that the chemical compounds of Iizuka had a credible, specific and substantial utility, i.e. the imidazole derivative compounds inhibit an specific enzyme, thromboxane synthetase, in human and bovine microsomes, a skilled artisan cannot reasonably conclude that the claimed polynucleotides have a specific and substantial utility or a well-established utility in view of the evidence presented.

On page 15 of the Brief, first paragraph and continuing on page 16, Appellants submit that the legal test for utility simply involves an assessment of whether those of skill in the art would find any of the utilities described to be credible or believable. Appellants cite *In re Brana* in support of the argument that while further research and development may be needed, this does not preclude a finding that the invention has utility, and state that the Federal Circuit admonished the PTO for confusing the requirements under the law for obtaining a patent and those required for government approval to market a drug for human consumption. Appellants further cite *In re Angstadt and Griffin, Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* and *In re Wands* in support of the argument that a considerable amount of experimentation is permissible if such experimentation is routinely practiced in the art and that a patent need not to disclose what is well known in the art.

As indicated above, while credibility is not been questioned herein, for the reasons previously discussed, specifically (1) the complete lack of information as to the type of protein kinase encoded by the claimed polynucleotides, (2) the targets of the alleged protein kinase, (3) biological processes and/or disorders/diseases associated with the expression of the claimed polynucleotides, or lack thereof, (4) the

lack of an experimentally determined NEK-1 protein sharing a high level of structural homology with the polypeptide of SEQ ID NO: 4 (closest structural homology having NEK-1 activity is that of Letwin et al.; 54% sequence identity), and (5) the unpredictability of the art in regard to accurately determining function based on structural homology, one of skill in the art cannot reasonably conclude that the specification teaches how to use the claimed invention or that the asserted utility is specific and substantial since further research would be required to determine the type of protein kinase encoded by the claimed polynucleotides, which are its targets and biological function.

The Examiner acknowledges the findings in *In re Brana*, *In re Angstadt and Griffin*, *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, and *In re Wands*. However, the Examiner disagrees with Appellant's contention that the claimed invention has utility in view of these findings. While it is agreed that FDA approval is not a requirement for finding a compound patentably useful and that routine experimentation does not render an invention unpatentable, it is noted that in the instant case, the utility rejection was not applied to the claimed invention because it failed to comply with government requirements to market the invention for human consumption or because some routine experimentation is required to practice the claimed invention. Instead, the utility rejection was applied due to the lack of information as to its biological function/use as discussed in claim rejections under 35 USC § 101 above. Furthermore, in regard to *In re Angstadt and Griffin, and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, while it is agreed that in gene chip applications, human chromosome detection, and intron/exon splice junction detection, linking polynucleotides to a DNA chip or hybridizing polynucleotides to other polynucleotides is not undue experimentation, one of skill in the art cannot reasonably conclude that the additional research required to practice the claimed invention is merely routine experimentation in view of the complete lack of information as to (1) a correlation between the expression pattern of the claimed polynucleotides and a disorder/disease or a biological process, (2) a correlation between detection of the corresponding human chromosome or intron/exon splice junctions and a specific biological function or

disease/disorder, or (3) a correlation between mutations in the gene encoding the polypeptide of SEQ ID NO: 4 and disease. In regard to *In re Brana*, it is noted that "the expectation of further research and development" as recited in the decision by the Federal Circuit refers to additional research to determine if the invention is safe and effective in humans, which are FDA requirements for market approval, and does not refer to further research and development to determine how to use the invention, which is the case herein. In regard to *In re Wands*, while it is agreed that one need not to disclose what is well known in the art, it is noted that neither the specification nor the state of the art describe or provide any information as to (1) the specific biological function of the polypeptide encoded by the claimed polynucleotides other than to indicate that the polypeptide of the instant invention shares structural homology to protein kinases, (2) the targets (i.e. substrates) of the alleged kinase, (3) the biological processes associated with the alleged protein kinase or its targets, (4) the specific diseases associated with the alleged protein kinase, and (5) the mutations in the gene encoding the alleged protein kinase which are associated with disease. Since information which would enable one of skill in the art to practice the claimed invention is not known in the art, it is the specification which must provide the necessary information to enable the skilled artisan to practice the claimed invention.

On page 16 of the Brief, last paragraph, and continuing on page 17, Appellants indicate that while they are aware of the new utility guidelines set forth by the USPTO, the current rules and regulations are the patent laws set forth in 35 USC and the rules set forth in 37 CFR but not the Manual of Patent Examination Procedure (MPEP) set forth by the USPTO. Furthermore, Appellants argue that it is the job of the judiciary and not the USPTO to interpret these laws and rules. Appellants argue that there are no recent changes in either 35 USC § 101 or in the interpretation of 35 USC § 101 by the Supreme Court or the Federal Circuit which support the new utility guidelines set forth by the USPTO and submit examples of US patents in Exhibit M, N, O, and P, which, according to Appellants, do not comply with the new utility guidelines. While Appellants admit that each application is examined on its own merits,

Appellants conclude that holding them to a different standard of utility is a clear violation of due process due to the similarity in subject matter between the claimed invention and the inventions in US patents of Exhibit M, N, O, and P.

Appellants are reminded that the Examiner must examine a patent application according to the guidelines set forth by the USPTO as well as the MPEP, since the Examiner has no authority to disregard such guidelines or to apply her own interpretation of patent law in the examination of the application. Furthermore, as set forth in the guidelines and the MPEP, the guidelines were promulgated by the PTO in accordance with all applicable case law and thus are believed to be consistent therewith. While the Examiner acknowledges the US patents of Exhibits M, N, O, and P, as indicated in previous Office Action Paper No. 14 (Final Rejection), mailed on 12/17/2002 and Paper No. 18 (Advisory Action), mailed on 5/20/2003, each application is examined on its own merits according to the current guidelines of examination as set forth by the USPTO and a discussion on the utility of any polynucleotide claimed in such patents would require a detailed review of the record of each individual case, which would be improper herein. Finally, Appellants are further reminded that the Examiner has no authority to comment in regard to the legality of the new utility guidelines or the MPEP as set forth by the USPTO.

B. Are Claims 2-3 and 6-7 unusable by a skilled artisan due to a lack of patentable utility?

At the beginning of page 18 of the Brief, Appellants indicate that arguments detailed in section VIII(A) of the Brief are incorporated by reference due to the fact that it has been determined by the courts that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph have the same basis. Appellants argue that since claims 4, 11 and 12 have been shown to have a "specific, substantial and credible utility" as indicated in section VIII(A), the present rejections under 35 USC 112, first paragraph cannot stand.

As indicated by Appellants, a rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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